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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,798	05/29/2007	Tadashi Okamoto	03500.109684.	4676

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EXAMINER

STAPLES, MARK

ART UNIT	PAPER NUMBER
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1637

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07/29/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/591,798	Applicant(s) OKAMOTO, TADASHI	
	Examiner MARK STAPLES	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 May 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5-10,16 and 19-24 is/are pending in the application.
- 4a) Of the above claim(s) 21-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5-10,16,19 and 20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>02/02/2010</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendment of claim 1 and the cancellation of claims 2-4, 11-15, 17, and 18 in the paper filed on 05/05/2010 are acknowledged. Claims 21-24 remain withdrawn.

Claims 1, 5-10, 16, 19 and 20 are pending and at issue.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections and Rejections that are Withdrawn

Oath is Accepted

2. The declaration filed 05/29/2007 is accepted. The Office finds that Applicant's arguments are persuasive.

Sequence Rules Compliance

3. It is acknowledged that Applicant has amended the specification to be in compliance with sequence rules.

Claim Rejections Withdrawn - 35 USC § 102(b)

4. The rejection of claims 1, 5-7, and 16 under 35 U.S.C. 102(b) as being anticipated by Yu et al. (US 2001/0036632 published 2001) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

Claim Rejections Withdrawn - 35 USC § 103(a)

5. The rejection of claims 8-10, 19, and 20 under 35 U.S.C. 103(a) as being unpatentable over Yu et al. as applied to claim 1 above, and further in view of Wang (2000) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

New Rejections Necessitated by Amendment

New Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 5-10, 16, 19 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 1 recites a primer for "elongating the A-strand" which primer has a sequential base sequence which is found in the A-strand. In other words, The A-strand primer has a sequence identical to a sequence of the A-strand which is used for elongating the A-strand. It is unclear how this can be done as the shared sequences are identical and not complementary and it is unknown, not recited, and not disclosed in the specification as to how the A-strand primer will bind to the A-strand in order to initiate elongation.

9. The relationship in claim 1 of "a" partial A-strand region in the B-strand primer and "a" complementary partial A-strand sequence in the B-Strand is unclear and hence

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indefinite. There is no clear language indicating that the partial A-strand region in the B-Strand primer is complementary or in any other way corresponds to the partial A'-strand sequence of the B-Strand. In fact as each sequence is a partial sequence of the A-strand or a partial complementary sequence of the A-strand, the current claim language permits for the partial A-strand region in the B-Strand primer and the partial A'-strand sequence of the B-Strand to be mutually exclusive and non-complementary. It is unclear how a primer can elongate a strand for which the primer has no complement in that strand.

As claim 1 is indefinite, dependent claims 5-10, 16, 19 and 20 are also indefinite.

New Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 1, 5-10, 16, 19, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (US 2001/0036632 published 2001), Hamill (WO 2002/081743 published 2002 as submitted on the IDS, newly cited in this action), and Wang (2000).

Regarding claim 1, Yu et al. teach methods of detecting a nucleic acids (entire publication), comprising the steps of:

(1) preparing a single-stranded nucleic acid having plural partial and sequential base sequences to be detected (A-strand) and a single-stranded nucleic acid having a base sequence complementary to a base sequence of the A-strand (B-strand) (see any one of the single strands of Gene A, B, or C and multiple primers to each single strand in Figure 1 and noting the complements bind to these primers in step 1B);

(2) preparing nucleic acids as primers each having one of the plural base sequences to be detected, immobilizing the respective primers independently in separate regions on a substrate, and preparing a primer array in which the respective base sequences to be detected are distributed in the primer-immobilized regions (see Figure 1 steps 1A and 1B and claim 1);

(3) preparing a nucleic acid having a sequence complementary to a partial and sequential base sequence within the region between a 3'-end of the A-strand and the base sequence to be detected which is located nearest the 3'-end as a primer for elongating the B-strand (see Figure 1 step 1B and claim 1);

(4) performing PCR reactions using the A-strand and B-strand as templates, and using the primers immobilized on the substrate, and the primer for elongating the B-strand (see Figure 1 step 1C, see section 5. *PCR Reactions* beginning at paragraph 0093, and see claim 1);

(5) forming a hybridized product of a nucleic acid corresponding to the A-strand which has been elongated and amplified as a result of the PCR reactions and bound to the substrate and a nucleic acid corresponding to the B-strand which has been

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elongated and amplified and has not bound to the substrate (see successive steps 1C through 1E of Figure 1); and

6) detecting the base sequence to be detected by detecting the hybridized product in the respective primer-immobilized regions in the array (note the labels for detection in Figure 1 and see claim 1).

Regarding claim 1, Yu et al. teach at least two immobilized primers, dual immobilized primers, but do not specifically teach an [A-strand] primer having a [A-strand] sequence where the complement or part of the complement of the [A-strand] sequence is part of a [B-strand] (this is the reasonable interpretation of claim 1 in light of the indefinite recitations in the claim, as given above).

Regarding claim 5, Yu et al. teach washing after the PCR reaction (see paragraph 0063, especially the 3rd sentence).

Regarding claims 6 and 7, Yu et al. teach fluorescent CY3 or CY5 labeled primers for synthesis of the new strands (see paragraph 0066 and also see paragraph 0006 for labeled probes).

Regarding claims 9, Yu et al. teach fluorescence detection and teach detection with intercalators and/or minor groove binders (see paragraph 0083) which inherently interact with double stranded nucleic acid, but do not specifically teach fluorescent intercalators.

Regarding claim 16, Yu et al. teach quantitative detection (see paragraph 0007).

Regarding claim 1, Hamill teaches PCR reactions using dual primers, one immobilized [A-strand] primer complementary to a region of the target strand [A-Strand] and a solution based primer [B-strand containing a complementary region of the A-Strand] complementary to the 3' terminus region of the immobilized primer complementary having a 3' terminus region complementary to a solution based primer (see Figure 2 and see lines 6-15 on p. 22).

Regarding claim 1, Hamill does not specifically teach that [B-strand] primer is immobilized.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the PCR reactions using dual immobilized primers of Yu et al. by using the immobilized [A-strand] primer for one of the immobilized primers for PCR reactions as suggested by Hamill with a reasonable expectation of success. The motivation to do so is provided by Hamill who teaches that methods using the immobilized [A-strand] permit deduction of sample sequence information, specifically the deduction of whether a polynucleotide is present in the sample from a microbial infection, disease condition, or genetic disorder (see lines 12-15 on p. 22). Both Yu et al. and Hamill teach methods using immobilized primers for polynucleotide detection, and so it would have been further obvious to one of ordinary skill in the art to substitute the immobilized primer of Hamill for one of the dual immobilized primers of Yu et al. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

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Yu et al. and Hamill teach as noted above.

Regarding claims 8-10, Schmidt et al. teach fluorescently labeled probes hybridized to nucleic acids bound to arrays of distinct wells on a microplate and also teach fluorescent intercalators which bind to double stranded nucleic acids (see column 4 lines 1 to 8 and see *Intercalating Dyes* beginning at column 4 line 9) which can be detected with confocal microscopy (see column 4 line 50).

Regarding claims 19 and 20, Schmidt et al. teaches measurements in real time, that is intermittently (see column 3 lines 40-67), and where the nucleic acid detection are performed in the same well/container of a micro-plate (see column 4 lines 1 to 8).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of Yu et al. and Hamill by using confocal microscopy to detect fluorescent intercalators on arrays as suggested by Schmidt et al. with a reasonable expectation of success. The motivation to do so is provided by Schmidt et al. who teach that their methods result in improved detection of functional antisense agents and can simultaneously measure the kinetics of complementary nucleic acid strand hybridizations (see column 1 lines 1-53). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 02/12/2010 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-

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9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Staples/
Primary Examiner, Art Unit 1637
July 28, 2010